IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Roberto FAGNANI et al. Serial No.: 10/054,728 Filed: October 25, 2001 Title: THREE DIMENSIONAL FORMAT BIOCHIPS Group Art Unit: 1639 Examiner: Jeffrey S. Lundgren Confirmation No. 3521 Attorney Docket No.: 71726/6776	Certificate of Transmission/Mailing I hereby certify that this correspondence is being facsimile transmitted to the USPTO, transmitted via the Office electronic filing system, or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below: July 10, 2008 /James J. Schumann/ Date James J. Schumann Registration No. 20,856 Attorney for Applicant(s)

REPLY BRIEF

Mail Stop: APPEAL BRIEF - PATENT
Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants submit this Reply Brief in response to the Examiner's Answer mailed May 13, 2008.

Section 9.1

In response to the Examiner's argument in Section 9.1 of the Answer, Appellants point out that original claim 18 recited "a solid substrate having a top surface" upon which the plurality of hydrogel cells were bound. The examples teach microspotting the droplets of polymerizing hydrogel prepolymer onto glass slides (see paragraphs 0077, 0085 and 0096). It is well-known that glass slides are flat plates, and such is mentioned in paragraphs 0004 and 0063. Deposition is obviously carried out on the top and not the bottom surface of the flat plate, as recited in original claim 18.

This terminology is simply used for reference purposes for the description of the remainder of the claimed subject matter. The Examiner's preoccupation with this terminology is simply not understood.

Section 9.2

In Section 9.2, the Examiner admits that the primary reference of Sundberg differs from the claimed invention in not teaching hydrogel cells that are formed from an isocyanate-functional prepolymer comprising polyethylene glycol having a molecular weight of about 5000 and urethane linkages.

In addition, Appellants submit that Sundberg does not show "individual three-dimensional hydrogel cells" which protrude from the otherwise flat top surface of the substrate (see claims 1, 18, 31 and 46); in contrast, Sundberg coats the entire substrate with a film and then synthesizes oligomers at different regions across the surface of the coated plate. These are not individual, protruding, three-dimensional cells.

The Examiner's secondary reference to Braatz similarly teaches applying a uniform coating and emphasizes that the coating is "protein non-adsorptive" (see Title and abstract, line 3). The Examiner takes the position that it would be obvious to substitute the Braatz polymer for the polyacrylamide gel of Sundberg. The Braatz polymer is fashioned from a diol or polyol having a molecular weight between 7,000 and 30,000, and it is designed to coat medical devices for the purpose of rendering them resistant to protein binding.

The Examiner states that one would have been motivated to utilize the Braatz polymer to create the Sundberg arrays because Braatz discloses a polymer with hydroxyl functional groups. However, this is incorrect for not only does Braatz fail to teach a hydrogel made from polyethylene glycol having a molecular weight of about 5000 (claims 3 and 32), but there are no hydroxyl functional groups in isocyanate-capped diols or triols. Capping causes reaction with all these hydroxyl groups during the creation of the isocyanate end-capped prepolymers; this is the inherent structure of an isocyanate-capped urethane prepolymer. An excess of isocyanate is used to create a prepolymer (as in Braatz Examples I to IX) so the product has a desired isocyanate content. Moreover, once the polymer coating has been created on the object, all of the reactive groups, i.e. the remaining isocyanate groups, are caused to react with water by soaking the

coated article in water (see column 9, lines 11-29); it is in this fashion that the polymer is rendered protein-resistant. However, such soaking or other reaction would prevent subsequent attachment of binding entities, particularly protein binding entities (see claims 13, 31, and 41); this is the very purpose of the polymer coating of Braatz. As a consequence, one simply would not be motivated to substitute the continuous protein non-adsorptive coating of Braatz for the Sundberg polyacrylamide gel because it would be totally ineffective to allow in situ synthesis of oligonucleotide or peptide probes for there would be no initiation sites which are needed.

Section 9.3

In response to Section 9.3 of the Answer, Appellants do not dispute that Wagner teaches a protein microarray, but Appellants emphasize, as the Examiner admits, that Wagner creates a monolayer on the surface of a substrate; the patches are proteins which are immobilized on the monolayer. Thus, the Wagner microarray is a traditional two-dimensional microarray (see column 9, lines 63-65, column 16, lines 43-45, column 32, lines 45-46, and Examples 1 and 2 in column 38, for example). The only thing three-dimensional at all about the Wagner microarray is that the substrate need not be flat or entirely two-dimensional; it could have some topological features, as by the inclusion of walls or other barriers to separate the regions where the patches are created (see column 13, lines 51-58). For this reason, Wagner is no more relevant than is Sundberg.

It is the Examiner's position that it would have been obvious to substitute the protein-non-adsorptive coating of Braatz for the monolayer polymer patches of Wagner, which patches Wagner uses to immobilize proteins on the surface of the monolayer. As explained just above, the Braatz resultant material would be singularly ineffective for immobilizing probes on its surface. One would not "have a reasonable expectation of success in the combination" of the two functioning as a microarray, when the very essence of the Braatz coating is to provide a surface coating having unique properties that avoid problems associated with protein adsorption, which solution is provided by the creation of polymers having a "lack of interactiveness with physiological surfaces" (see column 9, lines 30-36 and lines 63-66). The Examiner has not made a prima facie case for combining these two references by simply stating that Braatz shows the success of coating surfaces with a polymer comprising an isocyanate-capped polyurethane

prepolymer, when the coated polymer surface taught by Braatz would be clearly unsuitable for the Wagner purpose.

Section 10.1

With respect to the Examiner's argument in Section 10.1, Appellants' examples spot microdroplets of the polymerizing solution onto the surface of a silanated glass slide (see Examples 1, 1A and 2 for instance) and originally claimed a plurality of hydrogel cells on the top surface of a solid substrate. It is well known and described in the specification that glass slides are flat. Support for claim recitiations need not be "photographic" in the description. The products of Appellants' examples are clearly individual three-dimensional hydrogel cells that protrude from the flat surface to which they are bound. It is simply not seen how Appellants are allegedly carving out some undisclosed feature, when this is the basic characteristic of all of the examples and indicated by the very title of the application that was filed.

Section 10.2

The definition of hydrogel the Examiner reproduced on page 9 of the Answer is taken from the very first paragraph of the Detailed Description (see paragraph 0039). Appellants' reference to the Wikipedia internet encyclopedia is merely to demonstrate that the definition set forth in the specification itself is fully compatible with the commonly understood dictionary definition. The definitive court ruling on this point is the en banc 2005 Federal Circuit decision in the case of Phillips v. AWH Corporation, et al. (415 F.3d 1303, 75 U.S.P.Q.2D 1321). In this decision, the Court stated:

> "…the specification is the 'single best guide to the meaning of a disputed term,' and that the specification 'acts as a dictionary when it expressly defines terms used in the claims…'"

On page 11, the Examiner reproduces the entire first paragraph of the detailed description. This is the definition of hydrogel that should be used; hydrogels are only glassy when dehydrated. As the very name indicates, a hydrogel contains a large amount of water. Nowhere in Sundberg does the word "hydrogel" appear. Nowhere in Sundberg is it stated that

the polymer is selected for its ability to absorb water or desirably has a capacity to absorb water.

Appellants do not dispute that Sundberg teaches the use of flat substrates. However, Appellants again emphasize, as the Examiner admits, that Sundberg's disclosure is to apply a continuous film to completely coat the substrate, not individual three-dimensional cells, on the flat substrate.

The Examiner's underlined and italicized reference to "gels" at the bottom of page 11 is not relevant to the polymer itself that is being employed as a film coating; the quoted statement is included as a broadened definition of the substrate to which the coating may be applied.

Although most of the Sundberg teachings are directed to thin polymer films, Sundberg does teach the application of a crosslinked amino-functionalized polyacrylamide gel to a glass plate. This is a gel, but it is neither a hydrogel, nor is it a plurality of individual three-dimensional hydrogel cells of an isocyanate-functional polymer comprising PEG and/or PPG having urethane linkages which cells protrude from the otherwise flat top surface. The argued substitution of the protein-non-adsorptive continuous layer of Braatz does not cure this deficiency. There is no *prima facie* case made for this combination of references. As pointed out hereinbefore, an attempt to utilize the Braatz protein-non-adsorptive layer would be inoperative as a base in Sundberg upon which to synthesize oligonucleotide or peptide probes.

With respect to the Examiner's arguments on pages 13 and 14 of the Answer, Appellants do not argue that Braatz does not teach the use of a hydrogel; Braatz indeed does. However, the Braatz hydrogel is of a different character than Appellants'; the very purpose of Braatz is to design a polymer of a character that renders it protein non-adsorptive as set forth in its title. As explained hereinbefore, the Braatz teaching is to eliminate all potentially reactive groups to render it protein non-adsorptive. Thus, Braatz not only similarly teaches a use of a continuous film, but it also teaches the design of a film which would be singularly unsuited for use in the Sundberg array where the objective is to build patches of oligonucleotide probes by chemical synthesis upon selected regions of the uniform film.

Appellants' statement to which reference is made in the middle of page 14 of the Answer, i.e. the sentence at page 12, lines 10-11 of the Appeal Brief, is simply misread by the Examiner.

Appellants' point was simply that Braatz and Sundberg are similar from the standpoint that they both teach coating with a thin, uniform film.

As Braatz's title clearly states, it teaches a film that is protein non-adsorptive; the unique properties are achieved by eliminating all of the reactive groups. Sundberg requires such groups as a base for synthesizing peptides or proteins in situ. Thus, Braatz is the antithesis of the type of polymeric resin coating that Sundberg requires.

The Examiner's argues on page 16 that the Braatz disclosure of a molecular weight of about 7,000 to about 30,000 constitutes a disclosure of the recitation of polyethylene glycol and/or polypropylene glycol having a molecular weight of about 5,000 (claim 3). It is submitted that this Braatz statement in combination with the Braatz working examples using polymers respectively of 7,000; 10,000; 20,000; 9,000; 32,000; and 8,000 MW does not fairly support the Examiner's argument and renders it fallacious.

Section 10.3

The Examiner's point 10.3 is apparently mistitled and intended to refer to the rejection as being obvious over Wagner in view of Braatz. As set forth hereinbefore, Wagner clearly discloses only two-dimensional arrays based upon a monolayer which is a single-molecule thick film (column 8, lines 47-48). Regardless of what those organic molecules are, they are clearly not three-dimensional cells at least 20 microns thick. Admittedly, Wagner discloses a long list of potential functional groups Y that might be incorporated for the purpose of attaching protein-binding agents; however, it is clear that Wagner does not teach Appellants' claimed three-dimensional hydrogel cells at least 20 microns thick. As pointed out above, Wagner is directed to two-dimensional arrays, which is abundantly clear from the overall description.

For the same reasons as pointed out hereinbefore with respect to its argued combination of Braatz with the disclosure of Sundberg, one wishing to create the Wagner microarray by employing monolayer patches which are a single-molecule thick and upon which proteins would be immobilized in such a two-dimensional array would not substitute the protein non-adsorptive coating of Braatz—which teaches away from creating Wagner's film upon which proteins can be immobilized (Wagner, column 9, lines 49-50).

The various rejections based upon combination with the unique, protein non-adsorptive polymer of Braatz et al should be reconsidered and withdrawn. It is urged that claims 1, 3, 5-7, 9, 10, 16-18, 31-35, 41-43 and 46 be allowed.

Dated: July 10, 2008

Respectfully submitted,

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